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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/754,115	01/07/2004	Timothy D. Hey	DAS-104XC1	8974

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EXAMINER	
KOSSON, ROSANNE	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 07/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/754,115	HEY ET AL.	
	Examiner	Art Unit	
	Rosanne Kosson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15 and 21-31* is/are pending in the application.

4a) Of the above claim(s) *3,9,11,13,15 and 26-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10,12,14 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on June 14, 2006 has been received and entered. Claims 1 and 12-15 have been amended. Claims 16-20 have been canceled. Claims 21-31 have been added. Claims 26-31 are withdrawn from prosecution as being drawn to non-elected inventions, as the elected invention is drawn to a method of controlling or inhibiting an insect using a composition comprising SEQ ID NOS: 34, 45 and 47. These new claims are drawn to methods of using different sequences. Claims 22-25 are examined to the extent that they read on the elected invention only, i.e., SEQ ID NOS: 34, 45 and 47. All other sequences are non-elected inventions, as discussed in the previous Office actions. Regarding amended claim 12, because it now reads on the elected invention, it will be rejoined with the claims under examination. Claims 3, 9, 11, 13 and 15 were withdrawn from prosecution in the previous Office action as being drawn to non-elected inventions (the status identifiers for these claims should be corrected to indicate that these claims are withdrawn). Accordingly, claims 1, 2, 4-8, 10, 12, 14 and 21-25 are examined on the merits herewith.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claim 12 is objected to because of the following informality. The claim appears to contain a typographical error. The protein of SEQ ID NO: 34, $XptA2_{XWi}$ (see claims 1 and 8), is written as $XptA2_{Wi}$. Appropriate correction is required.

Claim Rejections - 35 USC § 112, first paragraph

Claims 1, 2, 4-8, 10 and 14 are again rejected, and claims 12 and 21-25 are rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite that the insecticide of the claimed method includes forms of Proteins A, B and/or C that are any fragments (each of these proteins may be truncated at any position or positions) or any variants in which any number of amino acids at any positions may be substituted by conservative amino acid changes. No such variants or truncation fragments are disclosed in the specification. This rejection was discussed in the previous Office action.

Applicants have traversed the rejection, asserting that many potentiators of SEQ ID NO: 34 were successfully used and are disclosed in specification. Applicants also assert that many fragments and variants are disclosed in the scientific and patent literature. In reply, Applicants have not indicated by name and page number which fragments and variants of SEQ ID NOS: 45 and 47 that are potentiators are disclosed in the specification. Applicants have also not indicated which fragments and variants of SEQ ID NOS: 34, 45 and 47 have the required insecticidal, inhibitory or potentiating activity. Applicants have noted that a protein that is similar to the protein encoded by SEQ ID NO: 34 has known protease cleavage sites, and that when the TcbA protein was cleaved and used to treat Southern corn rootworm, rootworm activity increased (see p. 11 of the Remarks). As the rootworm is an insect (a type of beetle), this method does not appear to be a method of controlling or inhibiting an insect, and Applicants have not indicated which portions of SEQ ID NO: 34 are fragments that may be used in the claimed method. The cited portions of the PCT publications referred to by Applicants are

definition sections for the terms used in these specifications. No fragments or variants of the proteins used in the claimed method are disclosed. The other references cited by Applicants also do not disclose the fragments and variants used in the claimed method. Regarding Examples 9 and 10 of the Written Description Guidelines, these examples are not analogous to the instant case, as they do not deal with fragments or variants, but with polynucleotides that hybridize to a given polynucleotide under given stringent conditions (see Written Description Guidelines, pp. 35-40, http://www.uspto.gov/web/offices/pac/writtendesc.pdf). Additionally, in these examples, the given polynucleotide is novel and not obvious. SEQ ID NOS: 34, 45 and 47 are not novel; they are known genes. Also, the hybridization conditions of 6X SSC and 65° C are much more stringent for polynucleotide binding than Applicants' conditions of 0.1X SSC and 55°C. Particularly, the temperature of 55° C is not very stringent, as the Office considers a temperature of at least 65° C to be needed for high-stringency conditions, as reflected in the guidelines cited by Applicants. Thus, the cited examples do not demonstrate that Applicants have described fragments and variants of SEQ ID NOS: 34, 45 and 47 that may be used in the claimed method. Therefore, the rejection of record is maintained.

Claims 21-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the claims recite that the insecticide of the claimed method includes forms of Proteins A, B and C that have a size within a particular range and that are encoded by any polynucleotide that maintains hybridization for any length of time under medium stringency conditions (0.1X SSC, 0.1% SDS and 55° C) with the polynucleotide encoding

Proteins A, B and C. No such hybridization-maintaining polynucleotides are disclosed in the specification. Thus, one of skill in the art would have no idea which proteins and polynucleotides Applicants have in mind that they wish to include within the scope of the claimed invention. Also, one of skill in the art would have no idea which polynucleotides that maintain hybridization under the claimed conditions encode proteins that have the claimed activities, either as an insecticide or as a potentiator of an insecticide.

Consequently, there is no evidence that any representative species of such large and varied genera- polynucleotides that maintain hybridization under conditions of 0.1X SSC, 0.1% SDS and 55° C to polynucleotides encoding Proteins A, B and C - were in the possession of the inventors at the time of filing. To satisfy the written description aspect of 35 U.S.C. 112, first paragraph, for a claimed genus of molecules, it must be clear that: (1) the identifying characteristics of the claimed molecules have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed. Because no hybridization-maintaining polynucleotides to polynucleotides encoding proteins A, B and C are disclosed, the claims fail to satisfy the written description requirement.

Claims 1, 2, 4-8, 10 and 14 are again rejected, and claims 12 and 21-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of controlling or inhibiting an insect by contacting the insect with a composition comprising SEQ ID NO: 34, SEQ ID NO: 45 and SEQ ID NO: 47, does not reasonably provide enablement for a method of controlling or inhibiting an insect by contacting the insect with a composition comprising any truncation fragment or any conservatively substituted variant of any

or all of SEQ ID NO: 34, SEQ ID NO: 45 or SEQ ID NO: 47. Consequently, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection was discussed in the previous Office action.

Applicants assert that their comments regarding the written description rejection overcome this rejection as well and that the specification discloses many, many Examples and Tables reporting a very large number of various combinations of various proteins that were used according to the subject invention. Applicants assert that the use of variants is reasonable and known in the art, as evidenced by the references cited above. Applicants further assert that one skilled in the art could make conservative amino acid substitutions and test the proteins and that this experimentation is not undue. In reply, as discussed above, neither the specification nor the references cited by Applicants disclose fragments of variants of SEQ ID NOS: 34, 45 or 47 that may be used in the claimed method. As for Applicants' tables and examples, the rejection is that fragments and variants of the proteins used in the claimed method have not been disclosed. The number of combinations of different whole proteins that have been tested is not germane to this rejection. Using variants of proteins may be known generally, but the instant rejection is that variants of Applicants' protein in the claimed method are not known and have not been disclosed. As for making conservative substitutions in a known protein sequence and testing everything made, such experimentation is undue, because, as previously discussed, Applicants have not disclosed any fragments or variants that may be used in the claimed invention. No species of the claimed genera are disclosed, and no guidelines have been provided for making fragments and variants that retain the function or the activity of the native protein. Such species or guidelines would allow one of skill in the art to predict how the proteins of SEQ ID NOS: 34, 45 and 47 may be modified so that they may be used in the claimed

method. Thus, the experimentation to produce fragments and variations would be random, undirected, trial-and-error, and, therefore, undue. In view of the foregoing, the rejection of record is maintained.

Claim Rejections - 35 USC § 112, second paragraph

In view of Applicants' amendments to the claims, the rejections in the previous Office action are withdrawn.

Claims 12, 14 and 21-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite the term "maintains hybridization." Applicants claim a method of using proteins encoded by polynucleotides that maintain hybridization under the stringency conditions of 0.1XSSC and 55° C (medium stringency). It is not clear for how long the hybridizing polynucleotides maintain their hybridization- a fraction of a second, hours, days, etc. It cannot be determined if Applicants mean to claim polynucleotides that remain hybridized during the hybridization and washing steps or polynucleotides that remain hybridized during the hybridization steps only (a larger group). As a result, the metes and bounds of the claims are unclear. Appropriate correction is required. Applicants may add a definite time value or definite steps of the hybridization experiments during which the hybridizing polynucleotides do hybridize. Or, Applicants may use a different term that is definite.

Claim Rejections - 35 USC § 103

Claims 1, 2, 4-8, 10 and 14 are again rejected, and claims 12 and 21-25 are rejected, under 35 U.S.C. 103(a) as being unpatentable over Morgan et al. ("Sequence analysis of insecticidal genes from *Xenorhabdus nematophilus* PMFI296," Appl Environ Microbiol 67:2062-

2069, 2001) in view of Ffrench-Constant et al. (US 2004/0103455, which claims priority to US 60/425,672, filed on November 12, 2002), Duchaud et al. (WO 02/094867) and Kramer et al. (US 6,281,413). This rejection was discussed in the previous Office action.

Applicants have traversed the rejection, asserting that the specification discloses for the first time that toxins from *Xenorhabdus* can enhance the activity of toxins from *Photorhabdus* and visa versa and that toxin complex proteins from *Xenorhabdus*, *Photorhabdus* and *Paenibacillus* can be used interchangeably. Applicants assert that their statements in the specification have the effect of an expert declaration by each inventor. Applicants further assert that their results are surprising, because *Xenorhabdus* and *Photorhabdus* proteins do not have a high degree of sequence identity for corresponding potentiator proteins. The rejection is a hindsight rejection because the prior art could not have provided an expectation of success that the surprising new combinations of proteins would function together in advantageous new ways.

In reply, it is not clear which effect of an expert declaration Applicants are referring to. The specification is a disclosure like any other specification and is not special in any way. It is also not clear what Applicants mean by "advantageous new ways." The claimed method is a method in which two proteins (SEQ ID NOS: 45 and 47) improve the activity of a third protein (SEQ ID NO: 34). As discussed previously, the ability of SEQ ID NOS: 45 and 47 to improve the activity of a third protein is known and is, therefore, not a new way. Regarding surprising combinations and results, as discussed previously, Ffrench-Constant et al. disclose insecticidal proteins from *Photorhabdus luminescens* (see paragraphs 3-7), SEQ ID NO: 10 and 12, that have 100% sequence identity to SEQ ID NOS: 45 and 47, respectively. SEQ ID NO: 10 is the protein TcdB2, which has activity equivalent to that of the protein TcdB1 (see paragraphs 9 and 22). SEQ ID NO: 12 is the protein TccC3, which has activity equivalent to that of the protein TccC2 (see paragraphs 9 and 24). TcdB and TccC2 proteins are known to enhance the toxicity

of the insecticidal TcdA1 protein. Host cells expressing all three heterologous proteins are more toxic to insects than the same host cells expressing TcdA1 alone (see paragraph 7). TcdA1 and SEQ ID NO: 34 ($XptA2_{xWi}$) are similar in size (283 and 284 kDa, respectively) and length (2516 and 2538 amino acids, respectively), and both act on the same type of insects, insects that can be infected with parasitic nematodes. This common set of insect toxin genes may be the result of an ancient common ancestor or of gene exchange (see Morgan et al., pp. 2065, 2067 and 2068). The two proteins have 42% sequence identity (see enclosed alignment of SEQ ID NO: 34 and TcdA1, GenBank record no. AAF05542, from the GenBank web site). As disclosed in the claims, two insect toxin proteins with at least 40% sequence identity that differ in size by 60 kDa or less and that are both in the protein A class for type of toxicity would be expected to have the same activity. XptA2 and TcdA1 are both proteins that were known at the time of Applicants' invention, and one of ordinary skill in the art would have expected them to have the same activity. As previously discussed, cited references disclose that Protein A is from the genus *Xenorhabdus* and Proteins B and C are from the genus *Photorhabdus*. It would have been obvious to one of ordinary skill in the art at the time that the invention was made to control or inhibit an insect by contacting it with a composition comprising the proteins of SEQ ID NOS: 34, 45 and 47, because the prior art discloses that a protein having at least 40% sequence identity to each of these proteins has insecticidal activity, and French-Constant et al. disclose that SEQ ID NOS: 45 and 47 potentiate (enhance) the activity of a protein that is homologous to SEQ ID NO: 34. Additionally, claim 1 requires that the protein that has 40% sequence identity to SEQ ID NO: 34 be an insect toxin and that the proteins that have 40% sequence identity to SEQ ID NOS: 45 and 47 be potentiators. But the potentiator proteins may potentiate anything; they need not act on the protein that has 40% sequence identity to SEQ ID NO: 34. As a result, Applicants' results are expected, and they are not surprising.

In view of the foregoing, the rejection of record is maintained.

No claim is allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rosanne Kosson whose telephone number is 571-272-2923. The examiner can normally be reached on Monday-Friday, 8:30-6:00, with alternate Mondays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rosanne Kosson
Examiner, Art Unit 1653

rk/2006-06-21

Rosanne Kosson

ROBERT A. WAX
PRIMARY EXAMINER